In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-792V

(to be published)

LAURA and BOJAN KALAJDZIC on behalf of A.K., a minor child,	Chief Special Master Corcoran
Petitioners,	Dated: June 17, 2022
v.	
SECRETARY OF HEALTH AND HUMAN SERVICES,	
Respondent.	

Amber Wilson, Esq., Wilson Science Law, Washington, DC, for Petitioners.

Claudia Gangi, Esq., U.S. Department of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On June 13, 2017, Laura and Bojan Kalajdzic filed a petition on behalf of their minor son, A.K., seeking compensation under the National Vaccine Injury Compensation Program ("Vaccine Program").[2] Petitioners allege that A.K. developed narcolepsy and associated symptoms after receipt of two doses of the "FluMist" form of the influenza ("flu") vaccine on October 30, 2014, and December 2, 2014, respectively. Petition at 1, 3 (ECF No. 1).

[1] This Decision will be posted on the Court of Federal Claims's website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012)). **This means that the Decision will be available to anyone with access to the internet.** As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole Decision will be available to the public. *Id*.

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) ("Vaccine Act" or "the Act"). Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

I proposed (after the case's transfer to me in January 2021) that the matter could reasonably be decided on the record, and the parties have offered briefs in support of their respective positions. Petitioner's Motion, dated July 2, 2021 (ECF No. 84) ("Mot."); Respondent's Opposition, dated September 13, 2021 (ECF No. 88) ("Opp."); Petitioner's Reply, dated October 12, 2021 ("Reply"). Now, after review of the medical record, briefs, and multiple expert reports, I deny entitlement. Petitioners have not preponderantly established that narcolepsy can be caused by the relevant version of the flu vaccine. An almost-identical contention was addressed at great length in several prior actions, but rejected, and no new scientific findings are offered herein that would fill holes in the theory as previously identified.

I. Factual Background

Vaccination and Six-Month Period Thereafter

A.K. was born on March 16, 2006. *See generally* Ex. 12. He was eight years old and in good health when he received doses of the FluMist vaccines, intranasally, on October 30, 2014, and December 2, 2014. *See*, *e.g.,* Ex. 1 at 1.3. FluMist is a live attenuated influenza vaccine ("LAIV").[3] Ex. A at 5.

The record memorializes no reaction to the vaccination in the days or weeks immediately after *either* dose was received. Mrs. Kalajdzic, however, has asserted in a witness declaration that she specifically recalls a February 2015 school field trip that she participated in, noting that her decision to attend was motivated by the concern that by this time "[A.K.] had started to become withdrawn and was exhibiting mood changes in addition to his increased fatigue issues," and that she had been pleased that he seemed interested and lively during the field trip. Ex. 28 at 2 ¶ 13. She maintains that his symptoms were appearing well before that date. *Id.* at ¶¶ 8–12.

Nevertheless, it was not until April 13, 2015—over four months after administration of the second FluMist dose—that any arguably-related symptoms are mentioned in the treatment record. At that time, A.K. was taken to Dr. Hien Tran at High Desert Pediatrics in Albuquerque, New Mexico, with Petitioners reporting a one-week history of fatigue, weakness, poor sleep, and irritability. Ex. 3 at 17. No reference in this record is made to symptoms occurring any earlier. Despite an examination that revealed only nasal congestion in addition to the complained-of

[3] As noted in *Agnew v. Sec'y of Health & Human Servs.,* No. 12-551V, 2016 WL 1612853, at *3 (Fed. Cl. Spec. Mstr. Mar. 30, 2016), FluMist is a cold-adapted vaccine administered intranasally. It contains live, but attenuated (meaning reduced in virulence), strains of the wild flu virus. The formulation received by A.K. was trivalent meaning it contained three separate wild virus strains. *See Dorland's Illustrated Medical Dictionary* 1940 (33rd ed. 2020) ("*Dorland's*"). To achieve an immune response from the body's adaptive immune system, the viral strains contained in the vaccine replicate at a temperature consistent with that found in the nasal cavity, but not at the higher temperatures found elsewhere in the body. *Agnew,* 2016 WL 1612853, at *3. As a result, the strains can replicate sufficiently to produce the antibodies necessary to fight a wild infection, but not enough to cause infection.

fatigue, Dr. Tran's assessment was right otitis media (although the record provides no evidence for this determination), and he prescribed amoxicillin. *Id.* at 17–18.

A.K.'s symptoms persisted, however, leading Petitioners to bring him back to Dr. Tran on April 21, 2015, for further evaluation. Ex. 3 at 16. Sleep issues were not discussed at this time, and the records reflect the primary concerns were related to fatigue "for at least several weeks now." Id. Blood testing performed a few days later revealed the presence of an acute Epstein-Barr virus ("EBV") infection. Ex. 2 at 3. On May 4, 2015, Dr. Tran reassessed A.K. for ear pain (attributed in part to ear wax build-up), noting that "[t]here has been no associated fever, decreased appetite, difficulty sleeping, fatigue, fussiness, malaise, nasal congestion, runny nose or cough." Ex. 3 at 14.

Manifestations of Sleep-Related Problems

More time passed with no evidence of treatment or sleep concerns. Then, on December 17, 2015, A.K. returned to Dr. Tran with complaints of acute onset of depression that had been persistent for over eight months, *i.e.*, since approximately mid-April 2015 (although as noted above these symptoms are not evident from the contemporaneous record). Ex. 3 at 12. The symptoms were described as feeling blue/sad and tired and were associated with a lack of energy. *Id.* In addition, behavioral concerns that were deemed "[r]elatively new per mother" were also reported. Ex. 3 at 13.

Dr. Tran ordered multiple lab tests, all of which came back normal with the exception of positive evidence of ANA antibodies.[4] Ex. 2 at 3. Approximately two weeks later, on December 29, 2015, A.K. followed up with Dr. Tran with complaints of chronic joint pain. The medical history from this visit recorded a familial history of rheumatoid arthritis along with other autoimmune conditions. Ex. 3 at 11. Dr. Tran's assessment included "chronic fatigue and malaise," and he referred A.K. to a rheumatologist, Dr. Jennifer Soep (although Petitioners have acknowledged A.K. never saw Dr. Soep). *See* July 2, 2018 Status Rep. (ECF No. 18).

Several more months passed with no additional treatment. Then, on March 10, 2016 (now about fifteen months after administration of the second dose in December 2014), A.K. returned to Dr. Tran with complaints of "[u]ncontrollable falling asleep and losing tone suddenly [with] laughing." Ex. 3 at 10. Although it is not evident from this record what kind of exam was performed, if any, Dr. Tran's assessment was "[n]arcolepsy and cataplexy," and he referred A.K. to a pediatric neurologist. Ex. 3 at 10.

[4] ANA stands for antinuclear antibodies. *Dorland's* at 70. An elevated ANA can reflect the presence of some autoimmune disease process, although follow-up testing and analysis is required for confirmation. K. Pagana et al., *Mosby's: Manual of Diagnostic and Laboratory Tests* 80 (6th ed. 2018)

Narcolepsy Treatment

The Kalajdzics learned that there would be a five-month wait for a pediatric neurology appointment at the University of New Mexico Hospital (Petition at ¶ 14), so they made alternative arrangements for A.K. to be evaluated at Colorado Children's Hospital ("CCH") on May 27, 2016. Ex. 2 at 1. A.K. was there seen by neurologists Elizabeth Halperin, M.D., and Padmini Palat, M.D. Ex. 2 at 1–9. The record from this visit reveals Petitioners' concerns about several narcolepsy-associated symptoms (*e.g.,* daytime somnolence, cataplexy, etc.), which were reported to have begun in January 2015, "shortly after he received two Flumist vaccines at school." Ex. 2 at 2. Although (they reported) the positive EBV titers revealed by Dr. Tran's testing had been thought to potentially explain these symptoms, their persistence concerned Mrs. Kalajdzic, and after some research of her own she began to suspect A.K. might suffer from narcolepsy with cataplexy. *Id.* She also made mention of the positive ANA findings. *Id.* Based on an overview of the prior lab results and their own exam, Drs. Halperin and Palat assessed A.K. with narcolepsy with cataplexy. *Id.* at 6. A.K. was referred to the CCH Sleep Clinic for additional testing and evaluation. *Id.*

Nurse Practitioner Susan Hines conducted the initial sleep evaluation that month. She was now informed (contrary to the contemporaneous medical record) that A.K.'s symptoms began in the fall of 2014, with "sleepiness after the first dose and cataplexy after the second dose." Ex. 2 at 13. The Kalajdzics also noted the EBV findings from the spring of 2015, proposing that treaters had assumed (incorrectly) that this explained A.K.'s presentation. *Id.* at 14. Additional lab testing performed in May 2016 revealed the presence of the DQB1*0602 allele of the Human Leukocyte Antigen[5] (the "narcolepsy HLA"), which is believed to be highly associated with the condition, and elevated Antistreptolysin O ("ASO") titers, which are also similarly associated. *Id.* at 2, 21. Based upon the foregoing, NP Hines's impression confirmed the earlier narcolepsy diagnosis, and she added the opinion that the FluMist vaccine likely explained its cause (although this record does not set forth the basis for this opinion, which does largely seem to have relied on Petitioners' assertions about symptoms onset that are not reflected in the medical record). *Id.* at 16.

From this point on, A.K. underwent additional sleep studies and evaluations yielding results consistent with narcolepsy and cataplexy. Ex. 2 at 32, 38. A variety of medicinal treatments plus exercise were employed. *Id.* at 41. A.K. was later in the early fall of 2016 diagnosed with a depressive disorder thought to be secondary to his other sleep-related symptoms. *Id.* at 53. His narcolepsy-associated symptoms continued into 2017. Ex. 7 at 47 (May 2017 follow-up visit to NP Hines). It appears he continues today to suffer from narcolepsy. Ex. 28 (Second Declaration of Laura Kalajdzic) (ECF No. 41-2) at 1, 4.

[5] HLAs are polymorphic molecules that present foreign antigens (like what would be contained in vaccines) to the immune system. *Dorland's* at 103. Certain genes are responsible for encoding cell-surface HLA proteins that regulate the immune system through their presentation of antigens. *Id.*

II. Expert Reports

A. *Benjamin Hughes, M.D.*

Dr. Hughes, a pediatrician with expertise in sleep medicine, offered a single written report for Petitioners. Report, dated March 24, 2019, filed as Ex. 16 b (ECF No. 31-2) ("Hughes Rep."). He proposed the FluMist vaccine A.K. received was likely a substantial factor in causing his narcolepsy.

Dr. Hughes attended The University of Texas, Austin for his undergraduate degree, and The University of Texas Medical Branch for his medical degree. *See* Curriculum Vitae, filed Mar. 25, 2019 (ECF No. 31-3) ("Hughes CV") at 1; Hughes Rep. at 1. He then completed his residency in pediatrics, fellowship in sleep medicine, and fellowship in pediatric pulmonary medicine at the University of Colorado School of Medicine. Hughes Rep. at 1; Hughes CV at 1. He is an Assistant Professor of Pediatrics at the University of Colorado School of Medicine. Hughes Rep. at 1; Tr. at 7. He is licensed to practice medicine and is board certified in pediatrics, sleep medicine, and pediatric pulmonary medicine. Hughes CV at 2–3; Hughes Rep. at 1.

Type 1 narcolepsy, Dr. Hughes explained, is attributable to "the destruction of neurons located within the lateral hypothalamus" in the brain. Hughes Rep. at 6. Those neurons are responsible for producing hypocretin, a neurotransmitter that plays an important role in regulation of wake/sleep cycles. *Id.*; T. Scammell, *Narcolepsy,* 373 N. Engl. J. Med. 2654 (2015), filed as Ex. 25 (ECF No. 32-1) ("Scammell"), at 2657. Symptoms associated with narcolepsy include persistent daytime sleepiness, impaired REM sleep (which typically occurs during deep sleep periods), plus cataplexy—definitionally part of Type 1 narcolepsy, and featuring "sudden episodes of partial or complete paralysis of voluntary muscles" that can immediately occur in response to strong, usually-positive emotions (laughter or pleasure at seeing someone). Scammell at 2654. Being positive for the narcolepsy HLA is also associated with the actual development of narcolepsy, although several environmental triggers (in particular certain kinds of upper respiratory infections) are also thought to be causal. Hughes Rep. at 6.

The bulk of Dr. Hughes's report featured a summary of A.K.'s medical history relevant to the claim. Hughes Rep. at 1–4. He deemed A.K.'s pre-vaccination history "unrevealing"—which would include the approximately five-week gap between the two doses of flu vaccine A.K. had received in the fall of 2014. *Id.* at 2. By April 15, 2015, however, (A.K.'s first medical visit post-vaccination), Petitioners were reporting to treaters that A.K. had (as of the week before) begun to display the kind of fatigue that would be reflective of narcolepsy. *Id.* at 2, 4, 5.

Although at this time A.K.'s treaters suspected an ear infection to explain in part his symptoms, Dr. Hughes proposed that the diagnostic criteria for otitis media were not fully met—in particular because A.K. displayed no fever or other direct proof of ear structure inflammation. Hughes Rep. at 4.

Dr. Hughes similarly rejected the possibility that an EBV infection around that time had caused A.K.'s fatigue, noting that (a) EBV is not associated with narcolepsy, and (b) A.K.'s evolving symptoms went beyond mere fatigue, to include classic narcolepsy features like excessive daytime sleepiness or weight gain. *Id.* at 5. It was thus Dr. Hughes's opinion that had A.K. been more formally tested in the spring or summer of 2015, he would have been shown to meet the primary diagnostic criteria for narcolepsy. *Id.*

Thereafter, and over the next year, Petitioners more regularly had A.K. assessed for his symptoms, and by May 2016 he had tested positive for the narcolepsy HLA (which Dr. Hughes deemed the "narcolepsy gene"). Hughes Rep. at 3. A sleep test in June 2016 fully confirmed the diagnosis of type 1 narcolepsy, or narcolepsy with cataplexy. *Id.* at 4. Dr. Hughes embraced this diagnosis as proper given A.K.'s overall history. *Id.* at 1, 5–6, 7.

Dr. Hughes's report also addressed whether a LAIV version of the flu vaccine, like FluMist, could cause narcolepsy, although this aspect of his report was thin in comparison to his lengthier evaluation of A.K.'s medical history. *See generally* Hughes Rep. at 6–7. Narcolepsy, he explained, is believed to occur via an autoimmune process, either through the mechanism of molecular mimicry between foreign antigens and the hypocretin-producing structures on the hypothalamus neurons, in which antibodies produced in response to the antigens attack the self-structures, or through "bystander activation" as an indirect result of other ongoing infectious occurrences. *Id.* at 6; J. Mahlios et al., *The Autoimmune Basis of Narcolepsy,* 23 Curr. Opin. Neurobiol. 5 (2013), filed as Ex. 26 (ECF No. 32-2) ("Mahlios"). It has been specifically associated with a streptococcus wild bacterial infection, or an influenza A viral infection. Mahlios at 2.

Of most relevance herein is the fact that studies have shown that the H1N1 influenza virus has also been deemed likely causal of narcolepsy, via the mechanism of molecular mimicry. Hughes Rep. at 6–7; Mahlios at 2–3; G. Luo et al., *Autoimmunity to Hypocretin and Molecular Mimicry to Flu in Type 1 Narcolepsy,* 115 PNAS 52: E12323 (2018), filed as Ex. 27 (ECF No. 32-3) ("Luo"). Luo specifically observed Type 1 narcolepsy to be associated with at least two flu peptide sequences derived from the viral strain used in the Pandemrix vaccine (an adjuvanted H1N1 flu vaccine administered for a period in Europe and elsewhere—but not in the U.S.). Luo at E12330. Dr. Hughes emphasized that although researchers had at one time thought that Pandemrix's association with narcolepsy (which other studies he filed have established)[6] was most likely attributable to its adjuvant (included to boost the vaccine's immunogenicity), other comparable H1N1 vaccines had been similarly linked. Because FluMist *also* included a live attenuated strain of H1N1 influenza virus, it too could be causal, in Dr. Hughes's view. *Id.* at 6.

[6] As discussed below, the literature offered in this case to substantiate the link between Pandemrix and narcolepsy has been reviewed extensively in prior narcolepsy cases that *I have decided*, and I therefore do not repeat those citations herein.

Dr. Hughes otherwise had little to say in his opinion regarding the other causation test prongs applied in Program cases. He deemed an onset of anywhere of three to four months after receipt of the second dose of FluMist in December 2014 to be medically acceptable (Hughes Rep. at 7), but he did not elaborate on *why* the putative autoimmune process would take this long to unfold. He was more affirmative in stating that the time *after* onset it took for treaters to recognize that A.K. had Type 1 narcolepsy (and thus formally offer the diagnosis) was not unexpected, since it could be difficult to make the diagnosis. *Id.* at 5–6. He did not explain what in the record suggested that *in this case* A.K.'s narcolepsy was likely vaccine-caused.

B. *S. Sohail Ahmed, M.D.*

Dr. Ahmed, a rheumatologist with specific academic expertise in the study of vaccines and autoimmune conditions, prepared two additional reports for the Petitioners. Report, dated June 29, 2020, filed as Ex. 30 (ECF No. 47-1) ("First Ahmed Rep."); Report, dated May 4, 2021, filed as Ex. 43 (ECF No. 65-1) ("Second Ahmed Rep."). In the context of responding to the first report offered by Respondent's expert, he opined (consistent with Dr. Hughes) that A.K.'s Type 1 narcolepsy was caused by the FluMist vaccine doses A.K. had received.

Dr. Ahmed attended Johns Hopkins University for his undergraduate degree and the University of Texas at Houston for his medical degree. *See* Curriculum Vitae, filed June 29, 2020 (ECF No. 47-2) ("Ahmed CV") at 5; First Ahmed Rep. at 1. Dr. Ahmed has over 20 years of experience in academic and clinical research that facilitates translational approaches to drug development. Ahmed CV at 2; First Ahmed Rep. at 2. He currently serves as a medical and scientific consultant for pharmaceutical and vaccine-producing companies. Ahmed CV at 2; First Ahmed Rep. at 2–3. He has published several peer-reviewed articles on multiple topics including immune-meditated diseases, vaccine adjuvant safety, autoimmune diseases, immune mechanisms triggered by vaccination, autoantibodies linked to autoimmune diseases, and genetic susceptibility in patients developing autoimmune diseases. First Ahmed Rep. at 3; Ahmed CV at 6. He is licensed to practice medicine in Italy and Massachusetts and is board certified in rheumatology and internal medicine. First Ahmed Rep. at 3; Ahmed CV at 5–6.

First Report

Dr. Ahmed began with an extensive discussion of the nature of narcolepsy, elaborating on medical science's progress in understanding how a wild flu infection might be associated with it. First Ahmed Rep. at 4–5. He defined narcolepsy as a "rare brain disorder" attributable to dysfunction in the hypothalamus neurons responsible for producing hypocretin. *Id.* at 4. Dr. Ahmed deemed the need for an external trigger for narcolepsy to be "well-known"—although his report also accepted that the narcolepsy HLA is "strongly associated" with the condition, thus supporting the conclusion that individuals who experience it usually have some genetic predisposition. *Id.* at 4, 9.

An infectious trigger essentially instigates an inflammatory immune response leading to damage to the relevant neurons, thereby disrupting sleep regulation. First Ahmed Rep. at 4. And the wild flu virus has been reliably associated with triggering narcolepsy. Indeed, Dr. Ahmed noted, an increase in narcolepsy cases was observed after the 1918 Spanish Influenza Pandemic. *Id*. More recently, an increase in narcolepsy incidence was observed after the H1N1 2009 Pandemic, and the increase was specifically associated with the H1N1 wild virus strain. *Id.;* K. Edwards et al., *Narcolepsy and Pandemic Influenza Vaccination: What We Know and What We Need to Know Before the Next Pandemic? A Report from the 2nd IABS Meeting,* 60 Biologicals 1 (2019), filed as Ex. 38 (ECF No. 47-9) ("IABS Report"), at 3–4.[7] Reliable research thus associates the H1N1 flu virus strain with narcolepsy, and its pathogenesis as due to the infection-caused destruction of hypocretin-producing neurons. First Ahmed Rep. at 9.

In addition, many things are known scientifically about how a wild flu infection could gain access to the hypothalamus—with the infectious process possibly beginning in the olfactory neurons, moving from there to the brain. IABS Report at 4. (Notably, the IABS Report lists other hypotheses for narcolepsy's pathogenesis, but does not seem to favor one over another as the most likely explanation. *Id.*). Narcolepsy could also be mediated by an autoimmune process. First Ahmed Rep. at 5, 7.

Dr. Ahmed proposed such an autoimmune process could proceed via molecular mimicry (in which self-structure similarity to a foreign antigen can result in an immune-driven attack on both), but admitted that not only was mimicry a "common normal physiological function of the immune response" (but does not inherently produce disease), but admitted that the theory "falls to critique" because it fails to explain *why* or *how* a mimic can "break normal immune tolerance," or what role the innate, immediate immune response plays in an autoimmune disease. First Ahmed Rep. at 5–6, 7. Alternatively, "bystander activation"—a process in which non-specific immune cells are stimulated into inducing "pre-primed autoreactive immune cells to induce pathogenesis" was also a potential mechanism. *Id.* at 7. Ultimately Dr. Ahmed's report focused more on molecular mimicry as the relevant mechanism herein, and he maintained that "strong confirmation" that antigenic similarity between H1N1 amino acid sequence components and the human hypocretin receptors drives the disease had been provided by reliable scientific studies. *Id.* at 9; *see also* IABS Report at 4.

Dr. Ahmed next turned to the central question of whether vaccination could *also* trigger narcolepsy. He acknowledged at the outset that vaccines, by design, generally possess a "poor ability" to cause infection, to greatly reduce the possibility that the vaccine's viral components

[7] Dr. Ahmed's report cites the IABS Report (a product of the 2nd International Alliance of Biological Science ("IABS") as authored by "C. Siegrist," although that name appears nowhere in the filed article.

could replicate and (in the process) more closely mirror a full, damaging wild virus reaction. First Ahmed Rep. at 6. It is for this reason that vaccines are typically formulated with inactivated or attenuated wild virus components. At the same time, vaccines must stimulate *some* kind of immune response to be effective. *Id.* Thus, in Dr. Ahmed's view the possibility of an aberrant reaction to vaccination remains even though vaccines are engineered to be inherently less dangerous to the human immune system.

In particular, Dr. Ahmed noted that a specific form of flu vaccine—Pandemrix, an H1N1 adjuvanted flu vaccine—has been reliably associated with some narcolepsy "outbreaks" elsewhere in the world. First Ahmed Rep. at 8; IABS Rep. at 3–4 (citations omitted). Dr. Ahmed's own research had helped show that "specific H1N1 viral proteins . . . are known to have homology with hypocretin receptors, a putative target antigen for selective hypothalamic neuron loss." First Ahmed Rep. at 8; S. Ahmed et al., *Antibodies to Influenza Nucleoprotein Cross-React with Human Hypocretin Receptor 2*, 7 Sci. Translational Med. 294 (S2015), filed as Ex. 33 (ECF No. 47-4) ("Ahmed Study").

In this article, Dr. Ahmed and his co-authors examined the sera of 20 Pandemrix-vaccinated narcoleptic patients, noting that prior studies had suggested an increased risk of narcolepsy was specific to Pandemrix—but not other, highly similar adjuvanted H1N1 vaccines. Ahmed Study at 1, 10. The Ahmed Study's authors attempted to identify the specific mimic between protein sequences from the flu strain contained in Pandemrix and the hypocretin receptors, finding that there was a homologous flu nucleoprotein peptide, an antibody likely responsible for the cross-reaction, and that it was found in the studied patients. *Id.* at 2–3. However, the nucleoprotein antibody content found in individuals who had received different versions of the flu vaccine was lower. Ahmed Study at 4.[8] Thus, the Ahmed Study's findings are more specific to the Pandemrix vaccine than the causal capacity of the antigenic wild virus contents common to differently-formulated vaccines.[9]

Although the FluMist vaccine is not identical in formulation to Pandemrix, Dr. Ahmed nevertheless opined that it too could cause narcolepsy—and that the facts of A.K.'s medical history reflected this likely occurred here. First, because FluMist is a LAIV, it has a "key advantage" over an inactivated-virus vaccine, in that it has a "greater ability to elicit cellular immunity and activate the nonspecific innate immune system" without an adjuvant, since the live portions of the virus can elicit a strong immune reaction on their own. First Ahmed Rep. at 6, 7. The administration of

[8] FluMist was not one of the versions of the flu vaccine considered in the Ahmed Study.

[9] In addition, the IABS Report emphasized that it has been hypothesized that vaccination with Pandemrix only led to narcolepsy in places where "there was considerable circulation of the pandemic virus . . . before the vaccine was introduced," and that overall more confirming evidence was needed to deem the vaccine association reliable. IABS Report at 3, 6.

FluMist is thus inherently more likely to create the circumstances for an aberrant reaction than when receiving a comparable inactivated, but unadjuvanted, vaccine.

Second, Dr. Ahmed opined, the close temporal interval for the vaccine doses A.K. received likely played a role in further encouraging a strong immune reaction (that in turn could have produced an autoimmune cross-reaction). The doses were administered approximately a month apart, with the second dose prompting an "enhanced immune response" both from an innate and adaptive standpoint. First Ahmed Rep. at 7–8. Thus, even if Respondent were correct that the H1N1 vaccine antigen *alone* (without an adjuvant) could not induce narcolepsy in an otherwise-susceptible individual, the second dose of a LAIV like FluMist would inherently impact the immune response more strongly. *Id.* at 8. The two doses, in Dr. Ahmed's view, mirrored the "multiple triggering factors" that had been observed by research considering Pandemrix-triggered narcolepsy in a context of background H1N1 infections. *Id.*

In addition to the above, Dr. Ahmed attempted to rebut certain points raised by Respondent in reaction to Dr. Hughes's initial report. He disputed, for example, the contention that the FluMist vaccine version A.K. had received had proven to be immunogenically "weak"—and hence formulaically incapable of inducing a strong, aberrant autoimmune reaction. First Ahmed Rep. at 9. In fact, studies had proven unable to measure the antibody response to a LAIV like FluMist, making it speculative to propose *what* kind of immune response it elicited. *Id;* I. Shannon et al., *Understanding Immunity in Children Vaccinated with Live Attenuated Influenza Vaccine,* 9 J. Ped. Infec. Dis. Soc. 1:S10 (2020), filed as Ex. 37 (ECF No. 47-8) ("Shannon"). Shannon, however, more reflects a discussion of how LAIVs are intended to work (by eliciting cellular immunity/activation of T cells plus mimicking a natural infection's stimulation of an innate response) than a rigorous evaluation of the expected efficacy of this version of flu vaccine. Shannon at 3–4.

Dr. Ahmed also took note of the fact that there was an absence of alternative explanations for A.K.'s narcolepsy. A.K.'s onset occurred when he was eight—younger than the age of most patients who first experienced narcolepsy (12-25 years old, with a peak around 15). First Ahmed Rep. at 7; M. Partinen et al., *Increased Incidence and Clinical Picture of Childhood Narcolepsy Following the 2009 H1N1 Pandemic Vaccination Campaign in Finland,* 7 PLoS ONE 3:e33723, filed as Ex. A, Tab 15 (ECF No. 36-16) ("Partinen") (deeming onset before the age of ten "rare"). This alone made it unlikely, in Dr. Ahmed's view, that A.K.'s disease could be attributed to a natural, if unidentified, cause. And he otherwise provided a common objection often interposed by Program petitioners when responding to contrary epidemiologic evidence undermining their causation assertions (or when attempting to explain their inability to provide affirmative epidemiologic evidence supporting causation): that the rarity of the injury itself limited the "signal detection" power of most large studies. First Ahmed Rep. at 7. No study could ever eliminate the possibility of a vaccine as having caused the relevant injury to a specific, susceptible person.

In addition, Dr. Ahmed proposed that the timeframe for A.K.'s post-vaccination onset was medically acceptable. The medical record, coupled with witness statements, suggested that A.K.'s onset of initial symptoms (mainly tiredness) occurred in the early winter of 2015—since in mid-February of that year, Mrs. Kalajdzic "attended a field trip to validate A.K.'s claims of being tired all day at school," even though she did not seek care for his symptoms until two months later. First Ahmed Rep. at 10. Such an onset (which, if measured from the second FluMist dose in early December 2014, would be within 60 days) was reasonably consistent with what literature says about how narcolepsy can present—as well as Respondent's expert's contention that literature like Partinen supported a 40 to 67-day post-vaccination onset. First Ahmed Rep. at 10; Partinen at 5 (Table 1—"Clinical Findings" (deriving onset data on 50 studied subjects who received Pandemrix or a closely similar H1N1 flu virus vaccine)). It was thus in Dr. Ahmed's view an acceptable timeframe sufficient to implicate the vaccine. *Id.*

In any event, Dr. Ahmed maintained that it was "far from settled science" *when* narcolepsy symptoms would manifest post-trigger—with periods of between one or two months versus six or more all acceptable as established by reliable medical literature. First Ahmed Rep. at 10–11; F. Han et al., *Narcolepsy Onset is Seasonal and Increased Following the 2009 H1N1 Pandemic in China,* 70 Ann. Neurol. 410, (2011), filed as Ex. A, Tab 10 (ECF No. 36-11) ("Han I"). Han I, however, observed a four to six-month delay from a putative infection in the winter months to the following spring and summer, when the incidence of narcolepsy was highest. Han I at 414–15. Moreover, Han I's authors expressly stated that based on its own subjects, "H1N1 vaccination is not the culprit for increased narcolepsy onsets in China," further diminishing its value in providing a potential timeframe for onset after vaccination. *Id.* at 415. Dr. Ahmed proposed that a more abrupt onset would be seen in connection with adjuvanted vaccines—but here (and even though he maintained elsewhere in his report that the two-dose regime for a LAIV somewhat copied the impact of an adjuvant), it was nevertheless medically acceptable for the overall disease to have progressed via a "slower, gradual" course than what might be expected for an adjuvanted vaccine like Pandemrix. First Ahmed Rep. at 11.

Second Report

Dr. Ahmed's supplemental report purported to rebut, point by point, certain arguments that Respondent's expert's second report raised, although in so doing Dr. Ahmed ended up simply repeating many of his prior contentions.[10]

[10] Dr. Ahmed's "supplemental" report ended up exceeding the length of his initial report by several pages, rather than constituting a succinct response to specific issues raised in Dr. Dye's supplemental report. The second report was also two times as long as Respondent's expert's supplemental report, but repeated many prior arguments instead of adding detail to existing ones. A second report of this nature was unjustified and unnecessary—especially since the Petitioners had *already* submitted an initial report from Dr. Hughes.

First, Dr. Ahmed expanded on his prior contention that A.K.'s narcolepsy was unusual for someone of his age (thus making it more likely the vaccination was causal, given the H1N1 strain association). Second Ahmed Rep. at 1–2. He insisted that narcolepsy occurring in those under ten was "rarely observed," and that his citation to literature like Partinen for this contention was accurate. *Id.* at 2.

In fact, Dr. Ahmed purported that epidemiologic studies supported a higher incidence of narcolepsy during the H1N1 Pandemic for slightly older children, with children the same age as A.K. far less likely to develop it. Second Ahmed Rep. at 3; Y. Dauvilliers et al., *Age at Onset of Narcolepsy in Two Large Populations of Patients in France and Quebec,* 57 Neurol. 2029 (2001), filed as Ex. C Tab 2 (ECF No. 58-3) ("Dauvilliers"), at 2031–032 (narcolepsy "peaks" occurring in studied sample at 15 and then 35 years of age). And he undertook an extensive discussion of the findings of studies focusing on Type 1 narcolepsy in China, with the goal of showing that a young child possessing the narcolepsy HLA, like A.K., was far more likely to have developed his condition due to vaccination, since studies did not otherwise reveal a high risk in the very young. Second Ahmed Rep. at 4–5. (In fact, some of these articles squarely support—albeit only regarding the specific sample in question—Respondent's contention that narcolepsy onset was *not* uncommon in children the same age as A.K. *See, e.g.,* F. Han et al., *Presentations of Primary Hypersomnia in Chinese Children,* 34 SLEEP 5:627 (2011), filed as Ex. C Tab. 5 (ECF No. 58-6) ("Han II"), at 631 (three-fourths of Chinese sample group experienced Type 1 narcolepsy prior to the age of ten)).

Second, Dr. Ahmed reiterated his assertion that the one-month gap between A.K.'s receipt of FluMist doses had played a role in the purported pathogenic process they instigated. Second Ahmed Rep. at 5–7. In reaction to epidemiologic evidence referenced by Respondent's expert showing that large numbers of children also received FluMist according to the same schedule, but without any increased incidence of narcolepsy, Dr. Ahmed contended that the results of such studies cannot "preclude biological plausibility,"[11] since a vaccine-caused injury in inherently rare, and therefore large-scale evidence of vaccine safety on the population level can never "disprove" the possibility of a vaccine-narcolepsy relationship. *Id.* at 6. The theory that narcolepsy could proceed via an autoimmune process actually *predated* the evidence that more specifically associated the Pandemrix vaccine with it (in the context of the H1N1 Pandemic). *Id.* at 7. Ultimately, Dr. Ahmed deemed the two-dose, close-in-time vaccination schedule to raise the

[11] Plausibility is of course *not* the standard governing Vaccine Act claims. *Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019). Rather, any causation theory must *not only* be generally plausible, but must also be corroborated and supported with reliable evidence and constitute a reputable theory otherwise—and petitioners must ultimately make this showing with preponderant evidence overall. However, I do not take Dr. Ahmed's contention here to reflect an admission that he cannot meet the proper legal standard, but instead to conflate "plausibility" with likelihood, and hence in accordance with the standard. (I nevertheless find, as discussed below, that *overall* the evidence offered in this case to associate FluMist with narcolepsy does not rise above a level of plausibility—independent of Dr. Ahmed's intent when using the term.

possibility of an aberrant immune response, especially in a child with demonstrated genetic susceptibility, as here. *Id.* at 7.

Dr. Ahmed next discussed Respondent's expert's assertions about purported distinctions between the H1N1 vaccines components and what was found in the FluMist version. *See generally* Second Ahmed Rep. at 7–8. In the context of this argument, Dr. Ahmed contested the contention that the relevant formulation of FluMist from 2014-15 had been deemed ineffective in prompting an immune response (and therefore the impacts of the vaccine proposed by Dr. Ahmed would not be realized)—although the basis for his argument was highly confusing.

Thus, Dr. Ahmed agreed that for the 2014-15 flu season (the relevant timeframe in which A.K. was vaccinated), FluMist "was ineffective against the predominant A/H3N2 strain" that was prevalent (although he also argued that its efficacy was no worse than the normal, inactivated version of the vaccine that would be administered by injection). Second Ahmed Rep. at 7; L. Grohskopf et al, *Update: ACIP Recommendations for the Use of Quadrivalent Live Attenuated Influenza Vaccine (LAIV 4) – United States, 2018-19 Influenza Season*, 67 Morbidity and Mortality Weekly Rep. 22:643 (2018), filed as Ex. A Tab 8 (ECF No. 36-9) ("Grohskopf I"). He also seemed to accept that the LAIV version had not proven effective against H1N1. Second Ahmed Rep. at 7. However, he emphasized that "the peptide sequence in H1N1 influenza nucleoprotein that cross-reacts with the human receptor regulating narcolepsy" was also found in the H3N2 strain—meaning, in his estimation, that it could "trigger the same immune response as the H1N1." *Id.* at 7–8.

Why this would be so, when Dr. Ahmed's own research suggests that it is things *outside* of the viral strain that impact vaccine-narcolepsy causality far more than the strain at issue (in particular, a manufacturing process that results in higher nucleoprotein levels) is not clear. Otherwise, he maintained that vaccine efficacy generally did not preclude the possibility of an individual aberrant response—although this argument was in essence in equivalent to his same broader argument about the inability of large-scale epidemiologic studies to "disprove" the possibility of causation. Second Ahmed Rep. at 8.[12]

Dr. Ahmed then commented on his own research regarding narcolepsy—which Respondent's expert had noted did not involve FluMist specifically, but was instead focused on causation involving a wholly-distinguishable version of the flu vaccine never administered in the U.S., Pandemrix. Second Ahmed Rep. at 8–10. Somewhat ignoring Respondent's point (that the Ahmed Study *itself* only showed a limited association with a specific, but distinguishable, version of the flu vaccine), Dr. Ahmed focused on the fact that his research had more generally

[12] In fact, after FluMist's discontinuance for a period of time, it was again recommended (for the 2018-2019 season, but included a different H1N1 strain. Second Ahmed Rep. at 13. And it was the earlier strain—which was in the version A.K. received—that was relevant. *Id.*

demonstrated the narcolepsy-causing potentiality of a cross-reaction (facilitated by antibodies) between H1N1 strain-carrying flu vaccines—a pathophysiologic process that he deemed pertinent to FluMist as well. *Id.* at 8. In so arguing, he embarked on an extended explanation of the cross-reactive immune process, again finding significant that A.K.'s symptoms appeared after receipt of a booster dose of the vaccine, resulting in a "reactivation process." *Id.* at 9. Even though FluMist was not adjuvanted (like Pandemrix is), its LAIV character gave it, in his view, a similar "charged" capacity, especially in the context of ongoing exposure to the wild virus, as was thought to have occurred in the 2009 H1N1 Pandemic. *Id.* at 9–10. (In actuality, literature discussing that background exposure was specific to Europe. *See, e.g.,* Partinen at 1–2). This, plus the dosage schedule, made FluMist more likely to cause narcolepsy in a genetically-susceptible child. *Id.* at 14.

In addition, other factors meant that what Dr. Ahmed's own research showed about *how* Pandemrix had caused narcolepsy almost did not matter herein. For example, he proposed that "[o]rexin specific T cells" could be generated by a molecular mimicry-caused cross-reaction instigated by FluMist, even without need of the H1N1 nucleoproteins that were the subject of his research. Second Ahmed Rep. at 10. And A.K.'s demonstrated possession of the narcolepsy HLA enhanced the possibility that he would have a lowered threshold for how much foreign antigen was required to trigger an autoimmune cross-reaction. *Id.*

Turning more directly to the FluMist vaccine itself, Dr. Ahmed maintained that there was evidence directly connecting it to narcolepsy—although the support for this contention came from the Vaccine Adverse Event Reporting System ("VAERS"),[13] or case reports involving adverse events after receipt of LAIVs. Second Ahmed Rep. at 10–13 (citations omitted). In response to the critique that this kind of proof was (for purposes of determining causation) the "lowest form of evidence," Dr. Ahmed responded that "case reports and case series significantly contribute towards the progression of scientific and medical knowledge," deeming their "real-world" context a value over a "controlled clinical research environment." *Id.* at 10–11. Indeed, VAERS reporting had helped disclosed issues with an earlier version of the rotavirus vaccine. *Id.* at 11.

Dr. Ahmed admitted that of the 49 reports he found (in total) associating narcolepsy with the flu vaccine, many were distinguishable because they did not include sufficiently precise information about relevant factors, or involved an earlier flu season. Second Ahmed Rep. at 11–12. But he was able to identify five VAERS reports involving FluMist (one of which was specifically a report of A.K.'s experience) administered in the same timeframe, observing the factual similarities between those cases and this one. *Id*. at 12–13. He noted as well that reports of

[13] The Vaccine Adverse Event Reporting System ("VAERS") is a national warning system designed to detect safety problems in U.S.-licensed vaccines. *See About VAERS*, VAERS, https://vaers hhs.gov/about html (last visited June 6, 2022). It is managed by both the CDC and the FDA. VAERS monitors and analyzes reports of vaccine related injuries and side effects from both healthcare professionals and individuals.

an association had dropped since the 2013-14 flu season, but suggested that those reports that did observe an association either involved a LAIV like FluMist, or the receipt of several vaccines at once. *Id.* at 13.

Dr. Ahmed also disputed one item of literature offered by Respondent to show that the two-dose flu vaccine regimen was specifically *intended* for children, to guarantee vaccine efficacy (and thus not, as Dr. Ahmed proposed, a likely factor in enhancing the vaccine's potentially aberrant impact). Second Ahmed Rep. at 13; X. Lin et al., *Trends in Compliance with Two-Dose Influenza Vaccine Recommendations in Children Aged 6 Months Through 8 Years, 2010-2015,* 34 Vaccine 5623 (2016), filed as Ex. C Tab 8 (ECF No. 58-9) ("Lin"). Lin considered records for more than 2.6 million children who received some form of flu vaccine (whether a LAIV delivered intranasally or injected) to evaluate if dosage recommendations were met, finding that while full vaccination compliance had increased over the relevant timeframe, it generally remained lower than optimal. Lin at 5624, 5628. Dr. Ahmed argued in reaction that Lin did not distinguish between a nasally-administered vaccine, like FluMist, and the injected version—and since the former's LAIV formulation gave it an adjuvant-like immunologic impact, the risk of an aberrant response (in comparison to the unadjuvanted flu vaccine itself) had to be higher, especially for children like A.K. carrying the narcolepsy HLA. Second Ahmed Rep. at 13–14. Dr. Ahmed did not substantiate this contention with other evidence comparing the effects of the two versions directly, however.

Otherwise, throughout his supplemental report Dr. Ahmed reiterated prior points about the acceptable timeframe in which A.K.'s narcolepsy symptoms manifested. Although he felt FluMist could heighten the risk of narcolepsy in a person carrying the narcolepsy HLA for up to one year, he deemed the period of six months after vaccination generally to be the "the strongest risk period." Second Ahmed Rep. at 10. The case reports that stood as the best comparables to A.K.'s circumstances involved onset of one to three months—a timeframe that would include the 72-day onset of A.K.'s symptoms that Dr. Dye had seemed to embrace in his first report. *Id.* at 12–14.

C. *Thomas J. Dye, M.D.*

Dr. Dye was Respondent's sole expert, and he prepared two written reports. Report, dated September 23, 2019, filed as Ex. A (ECF No. 36-1) ("First Dye Rep."); Report, dated October 19, 2020, filed as Ex. C (ECF No. 58-1) ("Second Dye Rep.").

Dr. Dye is a practicing physician at Cincinnati Children's Hospital Medical Center. First Dye Rep. at 1. His clinical focus is on the assessment and treatment of neurologically based sleep disorders, including central disorders of hypersomnolence such as narcolepsy. He completed residency training in child neurology and fellowship training in sleep medicine at Cincinnati Children's Hospital Medical Center, where he is now an Assistant Professor of Pediatrics and Neurology. *See* Curriculum Vitae of Dr. Dye, filed Sept. 30, 2019 (ECF No. 36-19) as Ex. B ("Dye CV") at 2. He is board certified in Neurology (with a Special Qualification in Child Neurology) and Sleep Medicine through the American

Board of Psychiatry and Neurology. He has authored peer reviewed articles on the epidemiology, pathophysiology, and presentation of pediatric narcolepsy. First Dye Rep. at 1; Dye CV at 4–6.

First Report

Like Dr. Hughes before him, Dr. Dye devoted a large portion of his written report to reviewing facts from A.K.'s medical history. *See generally* First Dye Rep. at 1–3. He deemed it "quite clear" that A.K. was properly diagnosed with Type 1 narcolepsy. *Id.* at 3. He also (consistent with Dr. Hughes) rejected initial treater views that A.K.'s symptoms were either the product of an ear or EBV infection. *Id.* at 3, 4. At most, A.K.'s initial presentation was "non-specific," but he later began to display symptoms clearly reflective of narcolepsy, which diagnostic testing supported. *Id.*

Dr. Dye's report included a discussion of narcolepsy itself, and while it was consistent with what Petitioners' experts presented, there were some distinctions or nuances in Dr. Dye's emphasis. He opined, for example, that narcolepsy was not all that "rare," despite its overall-low prevalence. First Dye Rep. at 3. He agreed that it was attributable to a loss of hypocretin cells, likely resulting from an immune-driven process, and that external infectious triggers (comparable to those identified by Dr. Hughes) could instigate some process leading to narcolepsy. *Id.* But he also specified that T cells (rather than autoantibodies produced more directly in reaction to a viral or bacterial antigen) were the likely immune cell mediators responsible for the hypocretin destruction—although he otherwise accepted that the cross-reaction of these T cells with the relevant neurons could be the product of mimicry or bystander reaction in connection with an overarching, prior-in-time infectious process. *Id.*

In addition, Dr. Dye maintained that narcolepsy tended to follow a seasonal pattern of manifestation—with symptoms onset usually occurring in spring (which characterized A.K.'s experience) and peaking by mid-summer. First Dye Rep. at 4; Han I at 414–15.[14] And he noted that wild H1N1 influenza infections were specifically understood to be associated with narcolepsy. First Dye Rep. at 4. A "marked increase" in individuals diagnosed with narcolepsy had been observed after the 2009 H1N1 pandemic, with diagnoses reducing in number once it subsided. *Id*; Han II at 630–31.

But Dr. Dye did not accept the contention that any vaccine containing some form of H1N1 wild flu virus strain would have the propensity to cause narcolepsy. Rather, reliable literature had observed an association *only* between narcolepsy and Pandemrix, an adjuvanted H1N1 flu vaccine. First Dye Rep. at 3; Partinen at 8 (50 out of 54 child narcolepsy patients had received Pandemrix within eight months of symptoms onset). Indeed, it was speculated in Partinen that the adjuvant itself (known as AS03 adjuvanted Pandemrix) might be causal. Partinen at 7. A smaller case-oriented study looking at 16 patients with narcolepsy had later demonstrated that *other* versions of the H1N1 flu vaccine could

[14] Dr. Dye even proposed that there was an association between narcolepsy and a patient's birthday, with some studies showing a particular correlation with March birthdays (and A.K.'s birthday was also in March). First Dye Rep. at 4 (citation omitted). But he acknowledged this was likely a coincidence.

also be associated with narcolepsy. Dauvilliers at 1428–429. But although the majority of the 16 subjects in Dauvilliers received a vaccine (14), 11 of the 14 received one that included the ASO3 adjuvant (and 7 of the 11 involved Pandemrix)—thus further seeming to implicate the adjuvant, or the Pandemrix version alone, as causal, as opposed to the wild virus component alone. *Id.* at 1429.

In the ten-plus years since such publications, a number of larger scale studies found *no* association between narcolepsy and any *non-adjuvanted* versions of the flu vaccine. First Dye Rep. at 5; T. Sarkanen et al., *Incidence of Narcolepsy After H1N1 Influenza and Vaccinations: Systemic Review and Meta-Analysis,* 38 Sleep Med. Rws. 177 (2018), filed as Ex. A Tab 16 (ECF No. 36-17) ("Sarkanen"), at 180, 185 (consideration of all published studies on topic through 2015, including ones from countries where Pandemrix was not used, revealed no elevated risk for narcolepsy associated with any vaccine other than Pandemrix). Sarkanen did cite Ahmed Study findings about the possible mechanism of antibody cross-reaction with hypocretin nucleoproteins as causal of narcolepsy, but noted that the role they played in Type 1 narcolepsy's pathogenesis "remains controversial." Sarkanen at 184.

Sarkanen also references a notable epidemiologic study highly relevant to this case, and Dr. Dye saw fit to offer it as well. First Dye Rep. at 5; Sarkanen at 180, 182; J. Duffy et al., *Narcolepsy and Influenza A (H1N1) Pandemic 2009 Vaccination in the United States*, 83 Neurology 1823 (2014), filed as Ex. A Tab 5 (ECF No. 36-6) ("Duffy"). Duffy attempted to assess whether there existed an association between narcolepsy and the version of the H1N1 vaccine administered in the United States, surveying 650,995 individuals in the United States vaccinated with the 2009 Pandemic vaccine, and 870,530 who received the seasonal vaccine. Duffy at 1823. Both the inactivated form of the vaccine and LAIVs were among the forms of flu vaccine received by the studied patients. None of the evaluated patients developed symptoms during the 180 days following vaccination, despite an expected incidence of 6.52. *Id.* In the 2010-11 seasonal flu vaccine study, only two subjects had onset of narcolepsy symptoms during the defined time period, compared to 8.83 expected. *Id.* at 1827. And out of the 45,246 individuals between the ages of 10 and 19 who received a LAIV, none developed narcolepsy despite an incidence rate of 3.84 per 100,000 individuals (meaning .83 cases of narcolepsy would have been expected). *Id.* Duffy's authors concluded that the forms of influenza vaccines in the United States containing the A(H1N1) virus strain could not be associated with an increased risk of narcolepsy, and also hypothesized that the antigens reflecting the relevant strain were not themselves likely to cause narcolepsy. *Id.* at 1823.

The fact that A.K. received FluMist (and not Pandemrix) was especially significant to Dr. Dye in concluding that the vaccine could not have been causal, since "no cases of narcolepsy have been linked to the FluMist vaccine." First Dye Rep. at 5. To the extent the H1N1 viral strain might be the cause of narcolepsy (rather than the ASO3 adjuvant in Pandemrix and comparable vaccines), that same viral strain was *also* contained in the FluMist formulation A.K. received—and yet studies like Duffy observed no LAIV-narcolepsy association. *Id.* Moreover, this form of the vaccine (like almost all flu vaccines administered in the U.S.) does *not* contain any adjuvant at all. First Ahmed Rep. at 6–7; First

Dye Rep. at 5. And Dr. Dye noted the existence of questions in medical science as to its overall effectiveness (contrary to Dr. Ahmed's argument later about the immunogenic power of a LAIV). First Dye Rep. at 5-6; Grohskopf at 643 ("[r]eview of LAIV effectiveness for previous seasons in the United States confirms low to no significant effectiveness of LAIV against influenza A(H1N1) pdm09-like viruses"). Dr. Dye thus deemed it a "highly dubious" contention that A.K. even received much exposure to this particular flu strain at all, let alone enough to trigger an aberrant reaction, further foreclosing the possibility that any association between narcolepsy and a Pandemrix version (containing both the relevant strain and adjuvant) would also be seen with FluMist.

Finally, Dr. Dye considered whether the timeframe for A.K.'s onset was medically acceptable. A.K. received his second dose of FluMist on December 2, 2014—and if his onset had begun close-in-time to his April 2015 initial treatment for unusual fatigue or sleepiness, more than 100 days would have passed since the vaccinations were administered. First Dye Rep. at 1–2, 4, 5. Yet even the best literature associating *some* versions of the flu vaccine with narcolepsy, like Partinen, only supported a post-vaccination onset interval (based on 50 patients) of 40-67 days. Partinen at 5, Table 1. Thus, A.K.'s onset occurred far too long after receipt of the December 2014 vaccine dose to be deemed reasonably associated. First Dye Rep. at 5.[15]

Second Report

Dr. Dye's second report contained responses to a number of specific contentions made by Dr. Ahmed. First, Dr. Dye disagreed that A.K. was younger than would be expected for a person with narcolepsy (and hence that it was more likely an unusual factor had caused it). Second Dye Rep. at 1–2. For this contention, Dr. Ahmed had relied on a proposed age range for narcolepsy derived from Partinen. Partinen at 1. But the purported range did not reflect an actual studied finding, and was more a summary of statements found in other papers—which in turn observed statistically-significant instances of onset *before* the age of 10. Second Dye Rep. at 1–2 (citations omitted). Indeed, a more recent 2017 study noted almost half of the cases evaluated for "pediatric" narcolepsy involved children experiencing onset at the age of eight or younger.[16] And Dr. Dye noted the existence of specific

[15] Dr. Dye also briefly touched on a possible alternative explanation for A.K.'s narcolepsy. He noted that A.K. had in testing revealed an elevated titer for an antibody specific to β hemolytic streptococcus, or "ASO". First Dye Rep. at 5; Ex. 2 at 16, 21 (referencing testing from May 2016). He maintained that elevations in the levels of this ASO antibody are associated with narcolepsy (leading researchers to conclude that streptococcal infections likely are a narcolepsy trigger. First Dye Rep. at 5; A. Aran et al., *Elevated Anti-Streptococcal Antibodies in Patients with Recent Narcolepsy Onset,* 32 SLEEP 8:979 (2009), filed as Ex. A Tab 2 (ECF No. 36-3). Although this contention is both tantalizing and finds some support in the record, however, I cannot conclude that preponderant evidence establishes this as an alternative cause for A.K.'s Type 1 narcolepsy—especially since the testing results were obtained a year after symptoms onset (whether in the winter or spring of 2015).

[16] Dr. Dye only filed the abstract for the relevant article, however, making it difficult to assess the reliability of the study in question. *See generally* Ex C Tab 5 (ECF No. 58-5) (specific citation omitted). But the more general point—whether narcolepsy onset at an age younger than ten is so uncommon that A.K.'s experience inherently suggests some unusual causative factor, like vaccination—was not specifically well-developed by Dr. Ahmed, given *other* evidence undercutting his contention, and thus my inability to fully analyze the persuasiveness of this article does not impact

pharmacologic treatments *intended* for children younger than ten experiencing narcolepsy. Second Dye Rep. at 2.

Next, Dr. Dye took issue with the Dr. Ahmed's emphasis on the significance of A.K's receipt of two FluMist doses, which Dr. Ahmed proposed had increased the likelihood of a pathologic response. Second Dye Rep. at 2–4. In Dr. Dye's view, there was nothing "unique" about the temporal scheduling of the doses, but rather that this schedule was recommended. *Id.* at 3; L. Grohskopf et al., *Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP) – United States, 2014-15 Influenza Season*, 63 Morbidity and Mortality Weekly Rep. 32:691 (2014), filed as Ex. C Tab 7 (ECF No. 58-8) ("Grohskopf II"), at 692. Indeed, a huge number of children received FluMist in the same two-dose regimen timeframe in 2014-15, when A.K. also was vaccinated—and a significant percentage of those children were (like A.K.) carriers of the narcolepsy HLA, but never developed narcolepsy. Second Dye Rep. at 3. Dr. Dye deemed this latter fact especially unsupportive of a vaccine association since it stood as direct epidemiologic proof of a kind. *Id.* at 4.

Dr. Dye relatedly attempted to bulwark his prior contention that the FluMist LAIV had proven to be ineffective immunologically (thus further undermining Dr. Ahmed's claim that the vaccine had an inherently high potential to be pathogenic). Second Dye Rep. at 4. He noted that the U.S. Influenza Vaccine Effectiveness Network had specifically observed in 2016 that a version of FluMist comparable to what A.K. received had only an efficacy of *three percent* for children—compared to a 63 percent efficacy of the inactivated flu vaccine for that same period. *Id.*; "ACIP Votes Down use of LAIV for 2016-17 Flu Season," CDC Newsroom, https://www.cdc.gov/media/releases/2016/s0622-laiv-flu.html (last visited June 2, 2022), filed as Ex. C Tab 11 (ECF No. 58-12) (the "CDC Article"). The CDC Article acknowledged Dr. Ahmed's point that the inclusion of the live virus in a LAIV was usually correlated with a stronger immune response, and was specific to a different season (2015-2016)—but also added that it followed "two previous seasons (2013-2014 and 2014-2015) showing poor and/or lower than expected vaccine effectiveness . . . for LAIV." CDC Article at 1. It was thus "unclear how the LAIV would be able to trigger an H1N1 based immune response leading to [Type 1 narcolepsy] when it was unable to trigger enough of an immune response to provide *any* degree of protection against *any* form of influenza." Second Dye Rep. at 4 (emphasis added). A.K.'s possession of the narcolepsy HLA did not change Dr. Dye's analysis, since a large percentage of the population carried it as well—but there was no observed increase in narcolepsy incidence in the relevant period. *Id.*

More fundamentally, Dr. Ahmed's own research showed why FluMist was not likely causal, when viewed from a mechanistic angle. Dr. Dye admitted that this research, associating the Pandemrix version of the flu vaccine with narcolepsy, "makes a very compelling case for antibody cross reactivity between influenza nucleoprotein specific to the Pandemrix vaccine and hypocretin neurons." Second

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my overall take on the point's evidentiary strength.

Dye Rep. at 4. But the very study setting forth these conclusions *also* observed that a comparable, but different, adjuvanted flu vaccine, Focetria, was *not* also associated with narcolepsy. Ahmed at 5; *see also* IASB Report at 4. And these two vaccines, in turn, were formulated and manufactured in a manner distinguishable from a LAIV like FluMist—further undermining the comparison to Pandemrix. Second Dye Rep. at 4.

Dr. Dye concluded with a fairly detailed discussion of Dr. Ahmed's contention that FluMist's method of administration (intranasally) presented a pathologic mechanism for how the vaccine could trigger narcolepsy. Second Dye Rep. at 5. Dr. Ahmed had proposed, as one possible mechanism, that a wild flu virus could theoretically "reach" the brain via the olfactory bulb, citing animal study research in support. *See* C. Tesoriero et al., *H1N1 Influenza Virus Induces Narcolepsy-like Sleep Disruption and Targets Sleep-Wake Regulatory Neurons in Mice,* PNAS E368 (Dec. 14, 2015), www.pnas.org/cgi/doi/10.1073/pnas.1521463112 (last accessed June 1, 2022), filed as Ex. 39 (ECF No. 48-1) ("Tesoriero"), at E369. But Dr. Dye contested the relevance of Tesoriero, noting that (a) it involved genetically altered mice as well as an exaggerated form of the virus not comparable to the attenuated flu vaccine, and (b) the hypocretin loss was *also* seen in the context of widespread neuronal damage throughout the brain. Tesoriero at E372–73.

As a result, the Tesoriero experiment did not, in Dr. Dye's view, offer a "model of narcolepsy," but instead reflected an influenza-caused encephalitis—an illness not at all comparable to the Type 1 narcolepsy A.K. had likely experienced (in which the *sole* damage at issue was to hypocretin receptors, with no other evidence brain harm or neurologic complications). Second Dye Rep. at 5. Indeed, the hypocretin receptor loss measured in Tesoriero was substantially less than what is seen in Type 1 narcolepsy. *Id.*; Tesoriero at E372–73. Dr. Dye more broadly disagreed, on similar grounds, with Dr. Ahmed's contention that a wave of narcolepsy in the years after the Spanish Flu Pandemic was likely wild virus-associated, nothing that the formal medical term at the time for the condition, "encephalitis lethargica," was not comparable to Type I narcolepsy, featuring many additional neurologic symptoms. *Id.*[17]

III. Procedural History

As noted above, this case was initiated in the early summer of 2017, approximately five years ago, and assigned to a different special master. After the filing of medical records was completed, Respondent offered a Rule 4(c) Report contesting entitlement in March 2018 (ECF No. 16). The following year, the parties began the process of obtaining expert reports, with the final report from Dr. Ahmed filed in May 2021. The month before (April 2021), the case was reassigned

[17] Dr. Dye also noted that there was doubt that the 1918 Pandemic even explained the subsequent narcolepsy-like condition observed in the 1920s, and that this view was supported by subsequent studies showing an absence of wild flu virus RNA in the brains of encephalitis lethargica patients from the time period. R. Dale et al., *Encephalitis Lethargica Syndrome: 20 New Cases and Evidence of Basal Ganglia Autoimmunity,* 127 Brain 1:21 (2004), filed as Ex. C Tab 13 (ECF No. 58-14).

to me, and I proposed a schedule for briefing ruling on the record. Since the filing of Petitioner's reply brief in December 2021, the matter has been fully ripe for resolution.

IV. Parties' Arguments

A. *Petitioners*

Petitioners maintain that they have preponderantly established that the FluMist vaccine can cause Type 1 narcolepsy and did so to A.K., given his established genetic susceptibility. Mot. at 4–5. After a summary of the expert opinions of Drs. Hughes and Ahmed and a short review of the relevant legal standards, Petitioners provided an argument for how they had satisfied each of the prongs in the causation test set forth in the Federal Circuit's decision in *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005). *Id.* at 6–29.

First, Petitioners assert that they established that the FluMist version of the flu vaccine can cause narcolepsy. Mot. at 6–19. They argue that in a susceptible individual (i.e., a person possessing the narcolepsy HLA) an external trigger can provoke circumstances sufficient to result in hypocretin interference, as proposed by Dr. Ahmed. *Id.* at 7. They note that wild virus influenza infections (in particular, the H1N1 strain) have been associated with narcolepsy, with some studies providing biological mechanisms for how this could occur—a foundation for the possibility that a vaccine incorporating such wild virus components, as here, could also be causal. *Id.* at 8–11, 13. A "vaccine safety signal" connecting receipt of specific versions of the flu vaccine with narcolepsy also began to be seen in passive surveillance reporting of adverse events. *Id.* at 11–12. A LAIV version of the vaccine, like FluMist, was likely to have a greater immunologic impact (given its similarity to a live infection), and even to mimic the impact of an adjuvanted vaccine, and thus could act as that trigger, based on Dr. Ahmed's explanation for how flu virus components are thought to relate to the hypocretin interference in the brain leading to sleep disfunction. *Id.* at 13–15.

Second, Petitioners posit that A.K.'s own medical history underscores that his illness was vaccine-caused. Mot. at 19–25. They maintain that the record in this case supports the following fact findings: (a) A.K. possessed the narcolepsy HLA, making him inherently more susceptible to the condition; (b) he was exposed to the FluMist vaccine at a young age, and when narcolepsy is less commonly observed; and (c) his receipt of two doses in a short timeframe increased the likelihood of an aberrantly robust immune response—sufficient under Dr. Ahmed's theory to provoke the biological mechanisms leading to narcolepsy. *Id.* at 20–24. Finally, they assert that A.K.'s onset was medically acceptable, when measured from his receipt of the last FluMist dose. *Id.* at 25. In this regard, they place earliest onset reflected in the records as February 12, 2015. *Id.* at 25–27. That timeframe was consistent with when post-trigger narcolepsy would be expected to manifest (within six months of exposure), independent of when the condition itself could be formally diagnosed. *Id.* at 27–28.

Petitioners' reply exceeded in length their initial 30-page motion. *See generally* Reply. Petitioners emphasize in it that the parties largely do not dispute facts specific to A.K.'s disease course, but instead disagree about the weight to be given certain evidence as it bears on causality. Reply at 1–3. They then reiterate prior arguments, addressing specific contentions contained in Respondent's opposition brief.

Regarding the first *Althen* prong in particular, Petitioners note Dr. Ahmed's credentials as bolstering the reliability of his opinion. Reply at 7–9. The opinion he offers is consistent with reliable science about narcolepsy, its likely pathogenesis, and its association with wild infections—as well as certain versions of the H1N1 flu vaccine. *Id.* at 10–14. Assertions by Respondent's expert that the association has not been preponderantly shown amount to requiring Petitioners to prove causation to a degree of scientific certainty—a standard that does not apply to Program claims—or to offer categories of evidence, such as epidemiologic proof, that are not required of Program petitioners. *Id.* at 15–21, 23–24. By contrast, Petitioners propose that case studies or passive surveillance reporting of post-vaccination narcolepsy are reasonable evidence supporting causation. *Id.* at 24–26. At bottom, Petitioners assert that their theory was reliable and sufficient to meet the Program's preponderant standard.

The Reply also seeks to address a fundamental issue raised by their claim: whether prior Program determinations on the capacity of FluMist to cause narcolepsy—which have been overwhelmingly unfavorable to the theory—suggest that this claim cannot succeed as well. Reply at 28–31. In reaction, Petitioners note that more recent studies, like the IABS Report, show that some combination of vaccination and background wild virus exposure is likely the explanation for prior narcolepsy "outbreaks," and that Respondent's arguments otherwise are applying a heightened standard of scientific certainty to evaluation of the theory. *Id.* at 31.

B. *Respondent*

Respondent offered a succinct brief in opposition to an entitlement determination in this case. After a summary of the medical history (Opp. at 3–7) and a review of applicable legal standards, Respondent specifically contends that the *Althen* prongs cannot be deemed satisfied given the evidentiary showing in this matter. The first, "can cause" prong, is not met in Respondent's estimation because FluMist was not reliably associated with narcolepsy—even if a wild virus strain contained in the vaccine has been, or where other forms of the vaccine are deemed connected. *Id.* at 12–14. Meanwhile, epidemiologic studies like Duffy, or meta-analyses like Sarkanen, discredit the conclusion that non-adjuvanted versions of the vaccine (like FluMist) are associated. *Id.* at 14–15. FluMist also was not found to be effective, undermining Dr. Ahmed's contentions about its high likelihood to promote a robust immune response. *Id.* at 15–16. Respondent highlights prior determinations in the Program (two of which I decided) that are highly relevant herein and suggest why denial of entitlement is appropriate. *Id.* at 16–18.

Respondent otherwise disputed the success of Petitioner's "did cause" showing, arguing that (a) A.K.'s possession of the narcolepsy HLA did not guarantee his development of narcolepsy, since others carry it but do not similarly experience narcolepsy after receipt of FluMist, (b) A.K.'s age did not make him a notable outlier in contracting the condition (and hence did not point to vaccine causation), and (c) the dosing schedule was a recommended part of the vaccination course —not a dangerous cofactor likely to contribute to a milieu in which an aberrant response was more likely. *Id.* at 18–20. And Respondent questioned whether an onset of narcolepsy in mid-February 2015, 72 days after receipt of the second dose (and without evidence of an initial reaction to the first) had been shown to be medically acceptable. *Id.* at 21–22.

V. Applicable Legal Standards

A. *Standards for Vaccine Claims*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[18] In this case, Petitioners do not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions;

[18] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*, 418 F.3d at 1278: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245.

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof" (citing *Moberly*, 592 F.3d at 1322)). And petitioners always have the ultimate burden of establishing their *overall* Vaccine Act claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Hum. Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Law Governing Analysis of Fact Evidence*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [ ] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (determining that it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Hum. Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical professionals; (ii) sick people attempt to honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs*., No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are accurate or superior on their face to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs*., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Hum. Servs*., 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). Under *Daubert*, the factors for analyzing the reliability of testimony are:

> (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for

> controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

In the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings, like the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs*., No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

Both parties filed numerous items of medical and scientific literature in this case, but not every filed item factors into the outcome of this Decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed

every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

E. *Standards for Ruling on the Record*

I am resolving Petitioners' claim on the filed record, and the parties have not challenged my determination to do so. Opp. at 1; Reply at 34. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers where (in the exercise of their discretion) they conclude that doing so will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The decision to rule on the record in lieu of hearing has been affirmed on appeal. *Kreizenbeck v. Sec'y of Health & Hum. Servs*., 945 F.3d 1362, 1366 (Fed. Cir. 2020); *see also Hooker v. Sec'y of Health & Hum. Servs*., No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided case on the papers in lieu of hearing and that decision was upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *Hovey v. Sec'y of Health & Hum. Servs*., 38 Fed. Cl. 397, 402–03 (1997) (determining that special master acted within his discretion in denying evidentiary hearing); *Burns*, 3 F.3d at 417; *Murphy v. Sec'y of Health & Hum. Servs.*, No. 90-882V, 1991 WL 71500, at *2 (Fed. Cl. Spec. Mstr. Apr. 19, 1991).

ANALYSIS

I. Prior Treatment of Narcolepsy Claims in Vaccine Program

There are a handful of reasoned Program decisions[19] involving claims that a vaccine caused narcolepsy—some of which were the product of cases before me. Hardly any have resulted in a favorable entitlement decision. *See generally A.T. v. Sec'y of Health & Hum. Servs.,* No. 16-393V, 2021 WL 6495241 (Fed. Cl. Spec. Mstr. Dec. 17, 2021) (HPV vaccine and narcolepsy); *Dougherty v. Sec'y of Health & Hum. Servs.,* No. 15-1333V, 2018 WL 3989519 (Fed. Cl. July 5, 2018), *mot. for review den'd,* 141 Fed. Cl. 223 (2018) (non-adjuvanted, inactivated flu vaccine and narcolepsy); *McCollum v. Sec'y of Health & Hum. Servs.,* No. 14-790V, 2017 WL 5386613 (Fed.

[19] Prior decisions from different cases do not control the outcome herein. *Boatmon*, 941 F.3d at 1358–59; *Hanlon v. Sec'y of Health & Hum. Servs*., 40 Fed. Cl. 625, 630 (1998). But special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Hum. Servs*., 76 Fed. Cl. 328, 338–39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the expertise and experience to know the type of information that is most probative of a claim") (emphasis added). They would therefore be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions.

Cl. Sept. 15, 2017) (non-adjuvanted, inactivated flu vaccine and narcolepsy), *mot. for review den'd,* 135 Fed. Cl. 735 (2017), *aff'd,* 760 F. App'x 1003 (Fed. Cir. 2019); *D'Toile v. Sec'y of Health & Human Servs.,* No. 15-085V, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) (FluMist and narcolepsy), *mot. for review den'd,* 2017 WL 2729570 (Fed. Cl. Mar. 2, 2017), *aff'd,* 726 F. App'x 809 (Fed. Cir. 2018).[20] Because the contentions in this case substantially replicate arguments made, and rejected, in these prior determinations (the most in-depth of which involve FluMist, as here), they warrant more discussion than might be appropriate in other contexts.

In *D'Toile,* I had the occasion to consider the scientific reliability and evidentiary persuasiveness of the theory that flu vaccines administered in the U.S. and containing the H1N1 influenza strain can provoke an autoimmune process that (via molecular mimicry) results in blockage of the hypocretin receptors in the brain responsible for sleep regulation, thereby producing narcolepsy. *D'Toile,* 2016 WL 7664475 at *20–24. I denied entitlement, however, because I determined that the version of the flu vaccine at issue—FluMist—could not (based upon the evidence presented) be reliably shown to cause narcolepsy as opposed to other, more well-studied forms such as Pandemrix. Not only was FluMist manufactured differently (and therefore contained fewer of the nucleoproteins proposed by some of the reliable literature to be the trigger for the autoimmune process leading to narcolepsy), but the expert testimony and literature offered in that case acknowledged (directly and indirectly) that the theory could not be reliably extended to cover the relevant form of the vaccine for other reasons. *D'Tiole*, 2016 WL 7664475, at *20–28. This was so even though the general theory that *certain formulations* of H1N1—containing flu vaccines can cause narcolepsy had reliable components. *Id.* at 20. At bottom, not enough evidence connected FluMist to narcolepsy in the same way. My decision was upheld at the Court and by the Circuit.

My determination in *McCollum* was consistent, although that case did *not* involve FluMist. Rather (and although proof of vaccination was itself a disputed matter in the case), the vaccine at issue was an H1N1-containing inactive, unadjuvanted version, akin to the version most often administered in the U.S. today. *McCollum,* 2017 WL 5386613, at *16. Nevertheless, I found the first *Althen* prong was not met, since (a) the most reliable literature on the subject implicated vaccine formulation or the inclusion of an adjuvant as the likely causal factors associating H1N1-containing vaccines with narcolepsy, and (b) a large-scale epidemiologic study directly

[20] One earlier reasoned decision was favorable to the petitioner. *See Garrison v. Sec'y of Health & Human Servs*., No. 14-762V, 2015 WL 7424016 (Fed. Cl. Spec. Mstr. Oct. 29, 2015). However, Respondent did not defend the claim—meaning the sole evidence before the special master in that case was the causation theory contained in Petitioner's expert report. *Garrison*, 2015 WL 7424016, at *1. In addition, the *Garrison* petitioner received the flu vaccine and then began experiencing sleepiness and related symptoms within a week or two—far sooner than even the earliest onset in this case. *Garrison*, 2015 WL 7424016, at *1–2. And *Garrison* contains no evaluation of the distinction between Pandemrix and the forms of flu vaccine administered in the U.S. There are also one or two cases in which the parties stipulated to damages, but no reasoned determination was made in those cases as to the persuasiveness or sufficiency of the petitioner's evidentiary showing.

undermined an association involving the unadjuvanted version. *Id.* at *17–19. This decision was also affirmed after two rounds of appeals.

II. Petitioners Have Not Carried Their Preponderant Burden

A. *FluMist Does not Likely Cause Narcolepsy*

This case largely if not wholly turns on whether the FluMist version of the flu vaccine can cause narcolepsy with cataplexy (also known as Type 1 narcolepsy). I find, based on the evidence before me, that it likely cannot. In so determining, I am unquestionably relying on my prior determinations on that topic—but that is because Petitioner's experts offer virtually the same theory and literature to support causation as was at issue in the prior relevant cases. Nothing published or determined since the time of my prior decisions has been identified in this case that would alter the analysis.

Petitioners' argument in this case mirrors closely the same rejected causation theory offered in *D'Toile.* There, as here, a claim was premised on the idea that findings specific to not just the adjuvanted version of the flu vaccine, but a *specific* version of that vaccine (Pandemrix) that was never offered in the U.S., could be transitively applied to FluMist—solely based on the flu virus strains common to both. But I rejected that premise—even though I acknowledged the reliability of research like that reflected in the Ahmed Study, which does persuasively provide a specific biologic mechanism for how hypocretin interference could cause narcolepsy. The problem with the theory is that it is too specific to Pandemrix, and thus cannot be then re-applied to a different vaccine formulation. IABS Report at 3, 6.[21] Dr. Ahmed's expert opinion in this case simply fails to address the implications of his own, otherwise-reliable study.

Admittedly, I decided *D'Toile* over five years ago—allowing for the reasonable possibility that more recent scientific or medical studies have "connected the dots" between what was then known about the Pandemrix-narcolepsy association and distinguishable versions of the flu vaccine like FluMist. But nothing filed in this case demonstrates this. On the contrary—the "meta-analysis"[22] Sarkanen, plus the IABS Report, are two more recent, comprehensive overviews on

[21] In addition, it remains possible that either the adjuvant included in the inactivated vaccine, or the background of the 2009 H1N1 Pandemic (with ample wild virus circulating in certain populations), played some causal role in sparking narcolepsy *independent* of the nucleoprotein cross-reaction proposed in the Ahmed Study. *See generally* IABS Report at 4. However, here (as in *D'Toile*), I make no determination as to the strength of alternative explanations for why narcolepsy cases might have seen an increased incidence in the context of H1N1 wild virus Pandemics.

[22] A meta-analysis is "any systematic method that uses statistical analysis to integrate the data from a number of independent studies." *Dorland's* at 1126. Admittedly, this kind of scientific study can reasonably be criticized as abstracting from studies with disparate methodologies, thereby potentially overstating the strength of the results of combined studies. *See,* e.g., *Dinh v. Sec'y of Health & Hum. Servs.*, No. 16-171V, 2022 WL 730258, at *11 (Fed. Cl. Spec. Mstr. Feb. 14, 2022). But at bottom, articles like Sarkanen or the IABS Report do set forth contemporary findings on the relevant subject—and overall they demonstrate *no individual recent scientific determinations* more supportive of Petitioners' theory than what was known previously.

what is known about causality in connection with narcolepsy, yet neither at all suggest that a FluMist-narcolepsy association has become any more likely than it was. Indeed, the IABS Report concludes with the sentence "[t]here are no clear associations observed between development of narcolepsy and *the other pandemic adjuvanted vaccines.*" IABS Report at 6 (emphasis added). It does not even bother to mention the lack of association with *non-adjuvanted* vaccines like FluMist, or LAIVs for that matter—since the latter contention simply has not been credibly explored. The Duffy epidemiologic study (while not perfect—as no such studies are) also strongly undermines the contention that versions of the vaccine other than Pandemrix are at all associated with narcolepsy. Duffy at 1823; Sarkanen at 180, 185.

Besides the above, Dr. Ahmed's other contentions regarding the unique nature of FluMist (and hence its additional capacity to cause a heightened, aberrant response) were contradictory or unpersuasive. First, the relevant research does not connect *all* adjuvanted vaccines with narcolepsy. *See, e.g.,* IABS Report at 6. Hence, the mere possibility that FluMist's LAIV character might approximate the immunologic effect of an adjuvant is wholly undercut by evidence (like Dr. Ahmed's own research) that connects primarily Pandemrix to narcolepsy, independent of adjuvants. Thus, why does it matter that FluMist can, in Dr. Ahmed's contention, replicate the immunogenic impact of an adjuvanted vaccine, when *that* factor is not the best explanation for why a particular vaccine is associated with narcolepsy?

Second, the evidence offered preponderantly establishes that FluMist was *intended* to be administered in a two-dose course, diminishing the persuasiveness of Dr. Ahmed's claims that this regimen was unusual or presented the opportunity for heightened risk. I have observed in many cases that the intended effect of vaccination (such as the fast stimulation of cytokine production, in the service of causing an adaptive response to the vaccine antigens) cannot simply be flipped to also demonstrate pathology, absent some evidence showing that the relevant factors *do* cause harm, or have been studied to that end. *D'Toile,* 2016 WL 7664475 at *24. The same is true here: a vaccine that sound medical science *directs* be administered in two, close-in-time doses is not *per se* more dangerous, immunologically-speaking, without some scientific or medical proof that this kind of temporally-close dosing produces bad outcomes of any kind. Dr. Ahmed is merely speculating that this could be a problem. Finally, it is not at all clear from the studies or other evidence filed in this case that narcolepsy is as rare an occurrence in children under the age of ten as Dr. Ahmed proposed—and hence I do not give A.K.'s age at time of onset any weight.

I also give little weight to the VAERS data or case reports filed in support of Petitioners' theory. The Program has generally not deemed VAERS data about associations between vaccines and injury to be especially probative (even if it does suggest a "signal" worthy of further evaluations). *Tompkins v. Sec'y of Dep't of Health & Hum. Servs.*, No. 10-261V, 2013 WL 3498652, at *16 (Fed. Cl. Spec. Mstr. June 21, 2013) (stating VAERS is a stocked pond because

it only contains reports of adverse events after vaccinations and does not consider data about the relative rate of these same events for unvaccinated individuals). Case reports otherwise do not establish causation, and thus are not a compelling substitute for the kind of evidence otherwise lacking herein. Indeed, as Dr. Ahmed admits, one of the relevant case reports in this case involves A.K.'s very circumstances—making it a particularly reflexive piece of evidence. Second Ahmed Rep. at 12.

None of the above reflects my determination that Dr. Ahmed's qualifications to comment on the matter at hand were lacking. Indeed, he has substantial personal experience relevant to the injury at issue, and his expert reports were fairly comprehensive (despite my overall finding that aspects of the opinion were not bulwarked with sufficient reliable proof). Portions of his opinion—the association between the H1N2 wild virus and narcolepsy; the same association with the Pandemrix version of the flu vaccine; and scientific theories about how an infection-caused cross-reaction could instigate the necessary hypocretin receptor damage—set forth reputable, tested scientific matters. But the opinion he offered *overall* did not provide me with reasons to conclude otherwise than I did in *D'Toile* or *McCollum*: that science that demonstrates a connection between a *different* form of the flu vaccine cannot be applied reliably to a LAIV like FluMist.

My rejection of a FluMist-narcolepsy association also does not reflect a mistaken substitution of a standard of scientific certainty in place of the Program's lower standard of preponderance. Indeed, even the reliable evidence I highlight herein associating *some* versions of the flu vaccine with narcolepsy does not amount to a showing at a level of certainty, as the IABS Report indicates—since there remains much to learn about narcolepsy causation. IABS Report at 5–6. Rather (and as in cases like *D'Toile*), I am observing that the overall chain of contentions that constitute Petitioner's theory has too many omissions and gaps to conclude "more likely than not" that FluMist can cause narcolepsy. At bottom, any association between narcolepsy and the flu vaccine is specific to a single vaccine version—not *other* versions (as other evidence offered in this case, like Duffy, underscores). And Petitioners' contentions about FluMist's capacity generally to prompt a robust immune reaction ultimately try to leverage what is known and expected about the vaccine into conclusions about its pathologic impact—but without any bulwarking evidence showing that FluMist does so. In fact, as Dr. Dye established, there is sound science suggesting that FluMist was *not* all that immunogenic.

More than five years have passed since my entitlement decisions on this topic issued, allowing medical science an opportunity to look further at the issue. Yet the more recently-published articles only underscore the degree to which the narcolepsy association remains specific to the Pandemrix version of the vaccine (as opposed to its component strains), or to background matters (such as vaccination in the context of an ongoing wild virus pandemic) not relevant to the facts of this case. It is thus—still—*unlikely* that FluMist can cause narcolepsy.

B. *Analysis of the Remaining Althen Prongs*

Although the disposition of this case turns almost wholly on the "can cause" prong, I will note my general conclusions with respect to the other two *Althen* prongs.

Regarding the second prong, the experts on both sides agree A.K. experienced Type I narcolepsy. But the overall record does not include sufficient evidence that would permit me to find that the FluMist vaccine likely *did cause* A.K. to experience narcolepsy. First, A.K.'s treaters never implicated the vaccine as causal. Ordinarily, treater opinions should be given some weight—although their speculation need not be deemed dispositive in any case, and I also note that given the insidious nature of narcolepsy, it is less likely that treaters would be "on the lookout" for vaccine causation under such circumstances in any event. Second, both parties agree that A.K. possessed the narcolepsy HLA, but this stands only as a risk factor associated with narcolepsy generally—*not* one associated with vaccination as the specific trigger. Medical literature was unsupportive of a vaccine association, with some articles looking at samples of children—a significant percentage who were also carriers of the narcolepsy HLA—who received the FluMist vaccine during the timeframe when A.K., but never developed narcolepsy. Grohskopf II at 692.

There is also little evidence of "challenge-rechallenge,"[23] that would underscore a vaccine reaction, since (a) A.K. experienced no demonstrated reaction at all to his receipt of the first FluMist dose, permitting no comparison to the degree of reaction to the second dose, and (b) there is no independent evidence of a faster or more robust response to the second dose. The fact alone that A.K. *eventually* experienced narcolepsy after the second dose, temporally, is hardly proof challenge-rechallenge.

The timing of A.K.'s onset (relevant to the third prong) was also problematic, although it presents a closer call. Here, onset occurred likely no earlier than two to four months after receipt of the second dose, depending on how that fact question is resolved. Ms. Kalajdzic's witness testimony that she had been noticing symptoms in A.K. as early as mid-February 2015 (thereby prompting her to attend a school field trip with him) merits weight. Moreover, since narcolepsy is not easily diagnosed, and can insidiously progress, it is wholly reasonable that Petitioners' first efforts to seek treatment in April 2015 do not demarcate temporally when A.K.'s symptoms began to manifest. Thus, an onset within six weeks to two months of the second FluMist dose is cognizable, and was not rebutted by Respondent—meaning in turn that it was preponderantly established.

[23] "A 'challenge/rechallenge' circumstance exists when a person has a reaction to one administration of a vaccine or drug and then suffers worsening symptoms after an additional administration of the same vaccine or drug." *R.S. v. Sec'y of Health & Hum. Servs.*, No. 15-1207V, 2021 WL 6502227, at *14 (Fed. Cl. Spec. Mstr. Dec. 15, 2021); *see also DePena v. Sec'y of Health & Hum. Servs*., 133 Fed. Cl. 535, (2017) (describing challenge/rechallenge as "when an individual ... exhibits a more severe reaction to a second administration of that vaccine").

But Petitioners' causation theory is unreasonably expansive about how long it would take for vaccine-caused narcolepsy to progress to obvious symptoms. Under their theory, *any* case of narcolepsy experienced by an individual within six months of vaccination, or even longer, could be attributed to that vaccination, assuming no other obvious intervening incidents that might undermine the conclusion that the vaccine was causal. This kind of open-ended timeframe is problematic for a Program case—especially where, as here, the underlying theory itself lacks sufficient preponderant heft. Prior cases have observed that some timeframes are simply too expansive in scope to be preponderant (in the absence of more specific evidence). *See,* e.g., *McCollum,* 2017 WL 5386613, at *22.

Here, I acknowledge Petitioner's preferred onset is better established than one later in time, and that temporal onset is consistent with Petitioner's theory, despite my questions about how reliable a timeframe it is. But because my disposition of the case mostly turns on the first *Althen* prong, success in determining the third makes no difference to the outcome.

III. The Case Was Properly Decided Without a Hearing

In ruling on the record, I am choosing not to hold a hearing—a determination that the parties largely accepted. Opp. at 1; Reply at 34. Determining how best to resolve a case is a matter that lies generally within my discretion, but I shall explain why I determined that a hearing was unnecessary.

Prior decisions have recognized that a special master's discretion in deciding whether to conduct an evidentiary hearing "is tempered by Vaccine Rule 3(b)," or the duty to "afford[] each party a full and fair opportunity to present its case." *Hovey*, 38 Fed. Cl. at 400–01 (citing Rule 3(b)). But that rule also includes the obligation of creation of a record "sufficient to allow review of the special master's decision." *Id*. Thus, the fact that a claim is legitimately disputed, such that the special master must exercise his intellectual faculties to decide a matter, is not itself grounds for a trial (for if it were, trials would be required in every disputed case). Special masters are expressly empowered to resolve fact disputes without a hearing—although they should only so act if a party has been given the proper "full and fair" chance to prove their claim.

This claim was fairly resolved without a hearing. Despite the extensive expert report filings, Petitioners' causation theory did not substantively "add" new or more persuasive evidence that would militate in favor of reconsidering my prior determinations on FluMist and narcolepsy, and hence I did not need to hear live from the experts. Indeed, my familiarity with these arguments and theories made a hearing even less necessary—many of the same items of literature I have evaluated in prior cases were offered in this one as well. *See, e.g.,* Partinen, Duffy. The most efficient means of resolving such a case is on the papers.

CONCLUSION

A Program entitlement award is only appropriate for claims supported by preponderant evidence. Here, Petitioners have not made such as showing. They are therefore not entitled to compensation.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court **SHALL ENTER JUDGMENT** in accordance with the terms of this Decision.[24]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[24] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.